DETAILED ACTION

Response to Arguments and Amendments

1. The response filed 8/11/10 has been entered.

2. Applicant's arguments filed 4/6/2010 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1, 4-17 and 38-40 are pending in this office action. Claims 2-3 and 18-37 have been cancelled.

5. Claims 1, 4-17 and 38-40 stand rejected under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 1-9, 11-13,15-25 and 27-33 of U.S. application No. 10/694,432 is withdrawn because the application is abandoned.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 4-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell (US Patent 6,265,386) in view of Pusztai et al. (US Patent 6,110,891) for the reasons made of record in Paper No. 20100511 and as follows.

Applicant argues in general that "The Campbell '386 reference describes methods for reducing hearing or balance loss, damage to ear cell, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and for prolonging survival in patients undergoing treatment with anti-tumor platinum coordination compounds, loop diuretics, aminoglycoside antibiotics, iron chelating agents, quinine, quinidine, or those exposed to toxic levels of noise or radiation" and that these methods comprise administering an effective amount of methionine. Applicant further argues that "the Campbell '386 patent does not disclose the administration of D-methionine.. to a cancer patient undergoing radiation therapy in need of reduction of oral mucositis."

Applicant also argues that Pusztai teaches treating mucosal cell damage by administering lectins.

In response Campbell teaches administering methionine to a population that is undergoing treatment with anti-tumor platinum coordination compounds (which would reasonably include cancer patient, see abstract) and Campbell specifically teach that D-methionine can be used to prevent other radiation side effects. Thus one of ordinary skill in the art would necessarily expect that cancer patients also undergo radiation treatment. Oral mucositis affects patients undergoing high dose chemotherapy and Campbell also teaches that exposure to radiation, whether intentional (as in radiation

therapy), or not, can result in gastrointestinal disorders (see col. 18, lines 7-10). As evidence by Raber-Durlacher et al (abstract) oral mucositis was developed in patients treated with chemotherapy (specifically cis-platinum, see page 367) wherein at least one third of patients receiving chemotherapy experienced oral mucositis (see page 371, rt. col.). Because this is a rejection under 35 USC 103(a), Pusztai was introduced to show that gastrointestinal disorders resulting from the administration of radiation may include the mouth (see col. 6, lines 13-15). Also Pusztai teaches the composition of diets for radiotherapy includes L-methionine (see Table 3, col. 18). Therefore one of ordinary skill in the art would have been motivated to administer L-methionine to reduce oral mucositis in patients undergoing radiotherapy. The claims broadly recite reducing oral mucositis in a human cancer patient undergoing radiotherapy, and the combination of Campbell and Pusztai makes it obvious to one of ordinary skill in the art to administer L-methionine to reduce oral mucositis in cancer patients undergoing radiation therapy.

Applicant's arguments have been fully considered but they are not persuasive for the reasons given above and that already made of record.

In Summary:

Campbell teaches a method of reducing gastrointestinal toxicity, in patients undergoing cancer chemotherapy (i.e., a cancer patient) and undergoing radiation therapy by administering the protective agents D-methionine, L-methionine, a mixture of D and L methionine and a pharmaceutically acceptable salt thereof (see col. 1, lines 12-35, col. 15, lines 25-30 and col. 19, lines 6-8, as required by instant claims 1, 4-6

and 13). Campbell also teaches that the methionine protective agent may be administered orally, and should be given in an amount that will result in a blood serum level equivalent to that achieved parenterally in doses ranging from 1.0 mg-500 mg/kg body weight. See col. 17, lines 44-47, col. 17, lines 30-56 and col. 24, lines 59- 65 (claims 13-17, 29-30).

Campbell also teaches the protective agent is administered from 6 hours before to 6 hours after exposure to chemotherapeutic agent, within 1 hour before and 1 hour after chemotherapeutic agent and one-half hour (30 mins) before and after chemotherapeutic agent (as required by instant claims 7 and 10-12, see col. 20, lines 8-24). Campbell also teaches that the protective agent may be administered simultaneously and or subsequently with radiation (see col. 19, lines 9-15).

As to the limitation of reducing oral mucositis, Campbell is silent to the specific teaching (i.e., regarding oral mucositis). Nonetheless Campbell teaches that these protective agents (i.e., D/L methionine or mixtures thereof) are employed to ameliorate radiation induced side effects such as gastrointestinal disorders, and that administration is orally.

However Campbell did not specifically teach reducing oral mucositis as required by the instant claims.

Pusztai et al. teach “Mucositis is a painful and debilitating condition in which rapidly growing epithelial cells are damaged and the external mucous layer is removed and/or not replaced sufficiently quickly”. Mucositis may result in infection by microorganisms which are present, for example in the mouth or gut. The condition is

seen as a major side effect in the treatment of cancer. The incidence and severity of mucositis may increase with increasing rounds of cancer therapy, and may ultimately effect patient treatment compliance and survival", (see col. 1, lines 55-54). Specifically Pusztai teaches that chemotherapeutic agents and radiotherapy are agents that damage the mucosal cells. Additionally Pusztai teaches administering a composition for radiotherapy includes L-methionine (see Table 3).

However Pusztai fails to teach reducing oral mucositis specifically. Nonetheless Campbell teaches generically treating mucusotis (see col. 9, lines 27-46)

Therefore it would have been obvious that Campbell's teachings of treating gastrointestinal symptoms in cancer patients would also reduce oral mucositis in a human or animal cancer patient undergoing chemotherapy because it is well known in the art that cancer patients undergoing chemotherapy and radiation are susceptible to destruction of the mucosal cell in the gut (gastrointestinal) and the mouth as evidence by Pusztai.

7. Claims 1 and 38-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell (US Patent 6,265,386) as evidence by Pusztai et al. (US Patent 6,110,891) for the reasons made of record in Paper No. 20100511 and as follows.

Applicant argues "Claim 38 is dependent on claim 1 and directed to a method of reducing oral mucositis wherein the patient is a cancer patient, is undergoing radiation therapy, and is undergoing treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound. Thus, claims 38-40 are patentable over

U.S. Patent No. 6,265,386 (Campbell) in view of U.S. Patent No. 6,110,891 (Pusztai) under 35 U.S.C. § 103(a) for at least the same reasons as claim 1".

In response both Campbell and Pusztai makes it obvious to one of ordinary skill in the art at the time the invention was made to reduce oral mucositis in patients undergoing chemotherapy and radiation because Campbell teaches that their patient population includes those who are being administered a platinum containing chemotherapeutic agent (see col. 18, lines 40-45) who are suffering from variety of cancers and which may include cancers that may result in side effects such as oral mucositis in the patient. Further Pusztai teaches that the composition comprising lectin is advantageous in controlling mucosal cell proliferation in patients undergoing chemotherapy and radiotherapy (see col. 8, lines 6-10). See also the response given above in para. 6 above.

Applicant's arguments have been fully considered but they are not persuasive for the reasons given above and that already made of record.

In summary: Campbell is applied here as above as it relates to claim 1.

Campbell further teaches that the chemotherapeutic effective amount of anti-tumor platinum coordination compound is cisplatin and the protective agent is D-methionine as required by instant claims 38-40, (see abstract).

As to the limitation of reducing oral mucositis, Campbell is silent to the specific teaching (i.e., reducing oral mucositis); nonetheless Campbell teaches that these protective agents (i.e., D/L methionine or mixtures thereof) are employed to ameliorate radiation induced side effects such as gastrointestinal disorders. As evidence by

Pusztai et al. "Mucositis is a painful and debilitating condition in which rapidly growing epithelial cells are damaged and the external mucous layer is removed and/or not replaced sufficiently quickly. Mucositis may result in infection by microorganisms which are present, for example in the mouth or gut. The condition is seen as a major side effect in the treatment of cancer. The incidence and severity of mucositis may increase with increasing rounds of cancer therapy, and may ultimately effect patient treatment compliance and survival", (see col. 1, lines 55-54). Specifically Pusztai teaches that chemotherapeutic agents and radiotherapy are agents that damage the mucosal cells, therefore it would have been obvious that Campbell's method involving oral administration of methionine would include reducing oral mucositis in a human or animal cancer patient undergoing chemotherapy because it is well known in the art that cancer patients undergoing chemotherapy and radiation are susceptible to destruction of the mucosal cell in the gut (gastrointestinal) and the mouth, as evidence by Pusztai.

Double Patenting

8. Claims 1, 4-17 and 38-40 stand rejected under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 1-29 of (US Patent 7,557,142) and claims 1-36 of (US Patent 6,187,817) for the reasons made of record in Paper No. 20100120 and as follows.

Applicant argues that "…claims 1-28 of the '817 patent are directed to a method for preventing or reducing ototoxicity, claims 29-30 are directed to methods of preventing or reducing weight loss, claims 31-32 are directed to methods of preventing

or reducing gastrointestinal toxicity, claims 33-34 are directed to methods of preventing or reducing neurotoxicity, and claims 35-36 are directed to methods of preventing or reducing alopecia" Further Applicant argues that "...because the claims of the '817 patent are not directed to reducing oral mucositis in a cancer patient undergoing radiation therapy, the claims do not include all the elements of subject claims 1 and 3-19".

In response Applicant's argument is found not persuasive because the claims of the patent '142 requires orally administering L-methionine to patients receiving chemotherapeutic agent which is also required by the instant application '436 by administering L-methionine. The conditions such as weight loss, reducing gastrointestinal toxicity etc., are all known conditions that occur when a patient is being treated with radiation and or chemotherapeutic agents. Since there is no separate defining step other than solely administering methionine, one of ordinary skill in the art would necessarily expect a reasonable amount of success in reducing these side effects when L-methionine is administered orally regardless of the patient population.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application is directed to treating diseases (reducing oral mucositis in a patient population undergoing chemotherapy and radiation) and the claims of in the instant claims '142 are directed to reducing the incidence of ototoxicity in a patient population undergoing chemotherapy with a chemotherapeutic effective amount of an antitumor platinum coordination compound (which is the same as in the instant claims). The claims of the '817 are directed to

reducing the ototoxicity in a patient population undergoing chemotherapy with a chemotherapeutic effective amount of an antitumor platinum coordination compound (which is the same as in the instant claims). Since there is no separate defining step other than solely administering methionine for the treatment of conditions related to the use of chemotherapeutic effective amounts of an antitumor platinum coordination compound, because the same population are being treated one of ordinary skill in the art would reasonably expect the different conditions to also be treated in a population experiencing the effects of the same antitumor platinum coordination compound, especially when radiation is commonly accompanied/combined with treatment of cancers (See evidence by Mori in its entirety).

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. V. G./
Examiner, Art Unit 1628
9/1/10

/Robert C. Hayes/
Primary Examiner, Art Unit 1649